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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 10/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/419,927	Sorensoen et al.
Examiner	**Art Unit**
Fozia Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Apr 9, 2002*.

2a) This action is **FINAL**. 2b) X This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *4-9* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *4-9* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

3 Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6 Other: _____

DETAILED ACTION

1. Receipt of Appellant's Brief and Supplemental Brief, filed on 05 August 2002 and 06 August 2002 in Paper Nos.14 and 15, respectively, is acknowledged.

2. In view of the Brief filed on 05 August 2002 in Paper NO:14, PROSECUTION IS HEREBY REOPENED. The amendment filed on 15 April 2002 is entered.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

3. Claims 4-9 are pending and under consideration by the Examiner.

4. The following previous rejections are withdrawn in light of Appellant's Brief, filed on 05 August 2002 in Paper No.14.

(1). The rejection of claims 4-9 made under 35 U.S.C. § 112, second paragraph.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly

5. Claims 4-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 4 which recites " a composition comprising a partially purified protein of extensin, said partially purified protein includes, rhamnogalacturonan proteins containing non-covalent bonds between hydroxyproline-rich glycoprotein and rhamnogalacturonan-1, said protein of extensin, lacks a tetra-hydroxyproline block and is in a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes", is vague and indefinite. Firstly, "*a partially purified protein of extensin*", is indefinite, because it is unclear how pure the claimed composition should be? Although instant specification asserts that "...extensin is partially purified from sugar beet pectin..", the degree of intended purity is not defined in the specification. Applicants must clarify the degree of purity intended for the claimed composition. Second, it is understood that the claimed composition should comprise partially purified extensin, however it is unclear what else should the claimed composition comprise, becasue it is not inderstooed how should the partially purified extensin protein also comprises other proteins, namely rhamnogalacturona protiens. Thirdly, the phrase "....rhamnogalacturonan proteins containing non-covalent bonds between hydroxyproline-rich glycoprotein and rhamnogalacturonan-1....", is confusing, because, it is unclear how many rhamnogalacturonan proteins are there. Instant specification defines rhamnogalacturonans as "the complex polysaccharide that is left after an endo-PG digestion, which has a major glycosyl composition", (see page 6), therefore, it is unclear whether rhamnogalacturonan is a protein or a

polysaccharide. Appropriate correction is required. Applicants must clarify all of the elements of the claimed composition.

Claims 5-9 are also vague and indefinite so long as they depend on claim 4 for the limitation set forth directly above.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 4-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a partially purified protein of extensin, which lacks a tetra-hydroxyproline block, does not reasonably provide enablement for a composition comprising a partially purified protein of extensin which lacks a tetra-hydroxyproline block, in a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims of the instant invention are drawn to a composition comprising a partially purified protein of extensin, said partially purified protein includes, rhamnogalacturonan proteins containing non-covalent bonds between hydroxyproline-rich glycoprotein and rhamnogalacturonan-I, said protein of extensin, lacks a tetra-hydroxyproline block and is in a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes. ***Amended claim 4 is not clear (see section 5 of this office action), therefore Examiner interprets claim 4 as a coompositon comprising a***

protein of extensin that lacks a tetra-hydroxproline block, in a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes.

Cytotoxic enhancement for lymphocytes is described on page 11, lines 10-15 of the instant specification as a method to enhance the cytotoxic activity of lymphocytes in relation to conditions of malignancy at tumor sites, intracellular infection, autoimmune diseases, and elimination of abnormal self-cells generated by the body itself. Therefore, "a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes", is interpreted as an amount of the claimed composition effective in treating these disorders, (i.e conditions of malignancy at tumor sites, intracellular infection, autoimmune diseases, and elimination of abnormal self-cells generated by the body itself).

Applicants disclose an oligo-cell experiments testing different pectins and combination of pectins and extensins in their ability to activate the survival and or proliferation of Tetrahymena thermophila cells (T- thermophila), (see page 12, lines 8-12). Applicants state that the similarities between T-thermophila cells and animal cells justifies the use of T. Thermophila cells as substitute for mammalian cells, (page 12, lines 11-20). Instant specification demonstrates that a combination of pectins and extensin increased cloning efficiencies of T-thermophila cells, and that partially purified extensin caused 80% cloning efficiency, (see page 13). However, instant specification does not demonstrate the claimed composition causes cytotoxic enhancement for lymphocytes. One can not reasonably, conclude that a composition that increases the cloning efficiency of T-thermophila cells *in vitro*, would cause cytotoxic enhancement for lymphocytes, thereby, would be therapeutically

diseases, and elimination of abnormal self-cells generated by the body itself, as claimed in the instant application. First, *in vitro* studies are not always predictive of treatment methods, and second, instant specification does not provide sound scientific reasoning why would an agent that increases cloning efficiency of these plant cells would be effective in treating these disparate diseases. Furthermore, these disparate diseases have different causes and symptoms, and involve many different processes and pathways, and it is not predictable that one agent would be effective in treating all of them. Thus, one of ordinary skill in the art would not predict that a composition that increases the cloning efficiency of T-thermophila would be effective in treating all of these disorders, without providing data to substantiate such assertion. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant application, Applicants did not disclose that the claimed composition was therapeutically effective to treat conditions of malignancy at tumor sites, intracellular infection, autoimmune diseases, and elimination of abnormal self-cells generated by the body itself. Furthermore, prior art of record is silent on the issue of a composition comprising a partially purified protein of extensin which lacks a tetra-hydroxyproline block that is therapeutically effective for cytotoxic enhancement for lymphocytes. Applicant is merely inviting the skilled artisan

extensin might be effective against the diseases mentioned above. In order to extrapolate from an *in vitro* experimentation to an *in vivo* methods of treatment, the *in vitro* experiments must be predictive of the *in vivo* administration, and instant specification fails to demonstrate that the *in vitro* experiments showing that a composition comprising pectin and extensin increases cloning efficiency of T-thermophila correlates to "a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes". Therefore, one of ordinary skill in the art would not reasonably conclude that a composition that increases the cloning efficiency of T-thermophila would be effective in causing cytotoxic enhancement for lymphocytes. Instant specification does not demonstrate that the claimed composition causes cytotoxic enhancement for lymphocytes, neither does it demonstrate that the claimed composition is in a "therapeutically" effective amount, i.e. effective in treating disorders such as malignancy at tumor sites, intracellular infection, autoimmune diseases, and elimination of abnormal self-cells generated by the body itself. Therefore, because of the unpredictability of the field, the fact that Applicants have not taught how to use the claimed composition in a therapeutically effective amount to enhance cytotoxicity of lymphocytes, the lack of guidance provided as to the correlation between the activation of T thermophila cells and cytotoxic enhancement of lymphocytes, and the lack of working examples, the instant specification is not enabling for a composition comprising a partially purified protein of extensin which lacks a tetra-hydroxyproline block, in a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes. Instant specification is only enabling for a composition comprising partially purified protein of extensin which lacks a tetra-hydroxyproline block.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7a. Amended claims 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (1989).

(A search for the definition of **rhamnogalacturonans** revealed: **(Pectin is the major component in plant cell walls and comprises about one third of the mass of the primary cell wall. The pectic polysaccharides comprise a family of acidic polymers like homogalacturonans (HG), rhamnogalacturonans, and several neutral polymers like arabinans, galactans and arabinogalactans attached to it).** Thus **rhamnogalacturonan is interpreted as being one of the polysaccharides found in pectin.** ***Amended claim 4 is not clear (see section 5 of this office action), therefore the Examiner interprets claim 4 as a compositon comprising a protein of Extensin that lacks a tetra-hydroxyproline block, in a therapeutically effective amount sufficient for cytotoxic enhancement for lymphocytes).***

Li et al disclose an Extensin isolated from sugar beet cell suspension which *lacks* the diagnostic tetra-hydroxyproline block, (abstract). The Extensin disclosed by Li et al is partially purified, (see page 328, column 2). The researchers disclose that the sugar beet Extensin shares a motif common with tomato Extensin p1 but differs by the position of an insertion sequence [X] in which the sugar beet Extensin splits the tetra-hydroxyproline block: Ser-Hyp-Hyp-[X]-Hyp-Hyp-

332). Therefore, the Li et al reference meets all the limitations recited in instant claims 4-9. With respect to the limitation that the claimed Extensin is in a therapeutically effective amount sufficient for cytotoxic enhancement of lymphocytes, the Li et al reference does not address this functional limitation, however, this functional limitation would be deemed inherent in the composition disclosed by Li et al. With respect to claims 7-9, the Extensin disclosed by Li et al is isolated from sugar beet, (page 328, second paragraph of column 2), therefore, it inherently comprises sugar beet pectin, sugar beet fiber and pectic polysaccharides, becaase "pectin" is a complex of colloidal polysaccharides found in the primary cell walls of dicotyledons, and since sugar beet is a dicotyledon it would inherently comprise these polysaccharides. In re Best (562 F.2d 1252, 1255, 195 USPQ 430,433-34 (CCPA 1977)).

In responding to the rejection of claims 4-9 made under 35 U.S.C. 102(b) as being anticipated by Li et al. (1989). Applicants argued that Li et al does not disclose all the elements of the claimed composition, because Li et al's composition does not have the claimed therapeutic activity. Applicants also argue that the Examiner does not address the specific limitations recited in claims 5, 7-9 , which are separately patentable, because these claims recite specific fiber or pectin sources for the composition of claim 4. (See Appellant's Brief filed on 05 August 2002 , page 7-9)

Applicants' arguments have been fully considered, but are not deemed persuasive. Firstly, Li et al discloses all of the elements of the claimed composition, explicitly or inherently. With respect to Applicants argument that Li et al do not disclosethe claimed therapeutic activity, is correct, however, this functional limitation would be deemed inherent in the composition disclosed

to Applicants' last argument, all the limitations recited in claims 5, 7-9 have been addressed by the Examiner. The Extensin disclosed by Li et al is isolated from sugar beet, therefore, it inherently comprises sugar beet pectin, sugar beet fiber and pectic polysaccharides, because "pectin" is a complex of colloidal polysaccharides found in the primary cell walls of dicotyledons, and since sugar beet is a dicotyledon, it would inherently comprise these polysaccharides, (recited in claim 5, 7-9).

Therefore Li's reference anticipates the instant claims 4-9 in the absence of any evidence to the contrary.

8. If Applicants wish to set up an interview with the Examiner or with the Examiner's supervise, Applicants are invited to call the numbers that appear at the end of this office action, which were also provided in the previous office actions.

Conclusion

9. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647